

Notice of Allowability

Application No.

10/767,824

Applicant(s)

COOPERSTONE ET AL.

Examiner

Raymond J. Henley III

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the application papers filed from 1/29/2004 through 12/21/2005.
2. ☒ The allowed claim(s) is/are 1-10.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).


* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 4/29/04; 8/13/04; and 5/11/04
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413B)
Paper No./Mail Date 012620061
7. ☒ Examiner's Amendment/~~Comment~~
8. ☒ Examiner's Statement of Reasons for Allowance/~~COMMENT~~
9. ☐ Other _____


Raymond J. Henley III
Primary Examiner
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EXAMINER'S COMMENTS/REASONS FOR ALLOWANCE

Comments

Applicants' Information Disclosure Statements filed April 29, 2004, (3 pages), May 11, 2004, (2 pages), and August 13, 2004, (1 page), have been received and entered into the application. As reflected by the attached, completed copies of forms PTO/SB/08A&B, the Examiner has considered the cited references.

Reasons for Allowance (First Action)

The following is an examiner's statement of reasons for allowance. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

The essence of Applicants' claimed invention are methods for treating or inhibiting hepatic fibrosis or cirrhosis in a mammal in need thereof, which comprises administering to said mammal an effective amount of CCI-779. The compound "CCI-779" was recognized in the art as the 42-ester of rapamycin with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid. In this respect, see the present specification at page 2, lines 15-19. This compound is depicted in the STN Registry document No. 162635-04-3 cited by the Examiner on the attached form PTO-892.

CCI-779 was well known to one of ordinary skill in the art as possessing several therapeutic activities. For example, Skotnicki et al., (U.S. Patent No. 5,362,718), as acknowledged by Applicants at page 2 of the present specification, line 18, teaches the preparation and use of CCI-779 and a variety of therapeutic activities for the compounds disclosed therein. Exemplary of such activities may be found at col. 6, lines 13-59 where it is

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disclosed that the compounds may be used in the treatment or inhibition of transplantation rejection including liver transplantation (col. 6, line 35). Other uses include treatment of tumors, fungal infections and proliferative disorders, such as restenosis.

The “parent” or “prototype” compound of CCI-779, i.e., rapamycin, was also well known in the art as possessing a plethora of therapeutic activities, such as having immunosuppressive effects and treating for certain types of cancers, (for the former and latter, see the present specification at page 1, lines 21-27), as well as for treating such diseases/conditions as lupus erythematosus, pulmonary inflammation, insulin dependent diabetes mellitus, skin disorders, such as psoriasis, bowel disorders, smooth muscle cell proliferation and intimal thickening following vascular injury (see the present specification at page 2, lines 6-14).

The closest art to the presently claimed invention appears to be the references cited in Applicants’ IDS filed August 13, 2004, which teach that (i) rapamycin, together with gamma interferon, shows an anti-fibrotic effect in immortal human hepatic stellate cells (Norikuni, reference HH); (ii) rapamycin reduces the expression of fibrosis-associated genes in an experimental model of renal ischemia reperfusion injury, (Jain et al., reference II); (iii) rapamycin and gamma interferon reduces transforming growth factor-beta-induced fibrosis in an organotypic slice culture, (Arisada, document JJ); rapamycin inhibits hepatic stellate cell proliferation *in vitro* and limits fibrogenesis in an *in vivo* model of liver fibrosis, (Zhu et al., document GG, cited in Applicants’ IDS filed May 11, 2004).

However, a review of all of the art cited in the case, both by Applicants and by the Examiner, fails to establish and convince the Examiner, with a reasonable degree of certainty, that the activity of rapamycin would be predictive of the activity of derivatives of rapamycin,

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including the claimed 42-ester of rapamycin with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid, or *vice versa*. It is recognized, as discussed above, that rapamycin and the claimed rapamycin derivative share some therapeutic activity, however such does not provide a *prima facie* adequate basis to conclude which other activities should be expected to be shared by these compounds. Ashraf et al., (U.S. Patent Application Publication No. 2004/0077677), appears to demonstrate this concept. In particular, At page 1, col. 1, paragraph [0005], the activities for rapamycin are set forth. In the following paragraph, the activities for the presently claimed 42-ester of rapamycin with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid are taught. What can be seen is that the presently claimed compound is taught to possess only a small subset of activities taught for rapamycin. Specifically, it is taught that, like rapamycin, the presently claimed compound is effective for ocular inflammation, malignant carcinomas, cardiac inflammatory disease and anemia.

This is not surprising given the unpredictable nature of the art of medicine and/or pharmacology in the area of therapy for disease treatment. Absent a reasonable suggestion that the derivatives of rapamycin, including the presently claimed, specific derivative of rapamycin, should be expected to behave in the same or similar manner as rapamycin itself over a substantial spectrum of activity, or a teaching or suggestion of which therapeutic activities should be expected to be shared, which would favorably include hepatic fibrosis or cirrhosis, the Examiner finds the presently claimed subject matter, at best, “obvious to try”, which has been well settled as an insufficient basis to rest a conclusion of obviousness under 35 U.S.C. § 103 upon, (see, for example, MPEP §2145(IX)(B), and the cases cited therein).

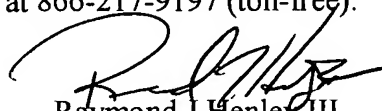
Accordingly, the Examiner finds claims 1-10 allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Raymond J Henley III
Primary Examiner
Art Unit 1614

January 26, 2006

EXAMINER'S AMENDMENT

An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview with Cathy Kodroff on January 26, 2006.

The application has been amended as follows:

In the Claims:

In claims 3 and 8, line 1, "wherein CCI-779 provided to said" has been changed to read - --wherein CCI-779 is provided to said---; and

In claim 10, line 1, "claim 1" has been changed to read ---claim 1 6---

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

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Raymond J Henley III

Primary Examiner

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January 26, 2006